US Army Medical Research and Materiel

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Recombinant Vaccine Against Botulinum Neurotoxin

This invention provides for the expression of synthetic genes that encode polypeptides containing protective epitopes of botulinum neurotoxins (BoNTs). When produced by *Clostridium botulinum,* BoNTs cause botulism by blocking the transmission of neuromuscular stimuli. The invention also includes a vaccine against botulism using the expressed polypeptides.

BoNTs are among the most toxic substances known, and only a few molecules are needed to abolish nerve cell activity, which can lead to respiratory failure and death. Humans are naturally affected by BoNTs via food poisoning, infant botulism, and wound botulism. Botulism poisoning could also occur during biological warfare or accidental laboratory exposure. Seven different antigenically distinct serotypes (A - G) of BoNTs have been characterized. Although polyclonal antibodies derived for a specific serotype can neutralize its toxic effects, they cannot cross-neutralize another serotype. The vaccine currently used against botulism is a pentavalent toxoid (i.e., serotypes A, B, C1, D and E). However, the vaccine is not only dangerous and expensive to produce, but also contains formalin, which causes reactogenic effects in recipients. The vaccine is incomplete as it only protects against serotypes A – E and requires four inoculations over 12 months. A more efficacious vaccine against all seven BoNT serotypes that will protect humans against natural, laboratory [illegible]ated, and biological warfare-related exposures is needed.

A new generation recombinant vaccine could alleviate many of the problems associated with the current culturing of large quantities of highly toxic *C. botulinum* and a dedicated current good manufacturing practices (cGMP) facility would not be needed. Additionally, the new vaccine would be purer, less reactogenic, more fully characterized, and cheaper to produce.

Features and advantages:

- **Expresses synthetic gene products encoding C-terminal ends of heavy chain fragments of botulinum neurotoxin**
- **Recombinant-BoNT protein fragment and plasmid products are completely nontoxic**
- **Large quantities have been expressed in the *Pichia pastoris* expression system**
- **Serotype B synthetic gene fragment protected mice, guinea pigs, and non-human primates**

Patent Status

and F synthetic gene fragments elicit protection in mice

Point of Contact

and G are in progress

Patent Application No.: 20030009025 Date Published: January 9, 2003
Available from: www.uspto.gov
Docket No.: RMED 99-29

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KEYWORDS: Vaccine; botulinum neurotoxin; fragment C; *Pichia pastoris*

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